

Can Nanoparticle Carrier Systems decrease the Reactivity of Porphyrinic Photosensitizers towards Serum and Cytosolic Proteins?

M. Vermathen¹, L. Sauser¹, I. Gjuroski¹, J. Furrer^{1*}

¹University of Bern

Since porphyrinic photosensitizers (PSs) can accumulate in diseased tissue, become only toxic when irradiated by light, and can transfer energy to oxygen forming highly reactive singlet oxygen, they have been used in Photodynamic therapy (PDT) of cancer and other non-cancerous diseases for several years. [1] Porphyrinic PSs of interest are usually hydrophobic structures and their intrinsic capability of self-aggregation in aqueous solution represents limiting factors, which reduce their PDT efficiency. Porphyrin conjugates have therefore become the focus of our current research to overcome these drawbacks, to increase the cellular uptake and ultimately the selectivity towards cancer cells. [2-3]

Part of the reasons for low productivity of anticancer porphyrinic PSs development is a limited knowledge about the mode, in which metabolic state the molecule penetrates the tumor cell and how much is inactivated. Given that porphyrinic PSs are administered intravenously, special consideration should therefore be given to interactions with macromolecular blood components. In this context, binding to the serum proteins albumin or transferrin on one hand, and to cytosolic proteins on the other hand, appear to be the most important issues, because such interactions determine also the deactivation of the PS, the excretion and differences in efficacy, activity, and toxicity.

In this contribution, interactions of a model porphyrinic PS, serine-chlorin e6 (SerCE), and of SerCE-PVP (polyvinylpyrrolidone) and SerCE-Kolliphor® complexes with the serum proteins albumin and transferrin and the cytosolic proteins cytochrome C, myoglobin, and ubiquitin have been investigated using NMR spectroscopy. The results reveal that the porphyrinic PS SerCE reacts immediately with the five proteins investigated, while PVP is able to prevent SerCE to react with those proteins, especially with albumin. The results with Kolliphor appear contrasting: the reaction is slow with myoglobin and immediate with albumin while reaction with the other proteins is also prevented. As such, the formation of nanoparticle systems with PVP seems to protect porphyrinic photosensitizers more efficiently than Kolliphor from interacting with proteins and may therefore promote intact cell entering of the PS.

[1] Heidi Abrahamse, Michael R. Hamblin, *Biochemical Journal*, **2016**, 473, 347 – 364.

[2] Marianne Hädener, Ilche Gjuroski, Julien Furrer, Martina Vermathen, *Journal of Physical Chemistry B*, **2015**, 119, 12117-12128.

[3] Ilche Gjuroski, Julien Furrer, Martina Vermathen, *Chimia*, **2015**, 69 (S 7-8), MC-151.